

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

REMARKS

Claims 28-59 are pending in the application, with claims 38-40 and 42 withdrawn from consideration. Applicant has amended claims 28, 30, 44, 48 and 50 and has added claims 60 and 61. Accordingly, claims 28-61 will be pending in the application upon entry of the amendments presented herein.

Independent claims 28 and 48 have been amended to point out more particularly the cancer treated by the methods. Claims 30, 44 and 50 have been amended to improve dependency and/or claim clarity. Claims 60 and 61 have been added to claim the invention more fully. Support for the claim amendments and additions can be found in the specification and claims as originally filed. No new matter has been added.

Unless otherwise specified, reference herein to a specification page number refers to the specification published as WO 2004/006966 (PCT/IB2003/002785).

Amendment of the claims should in no way be construed as an acquiescence to any of the rejections set forth in this Office Action or any previous Office Action, and was done solely to expedite prosecution. Applicant reserves the right to pursue the claims as originally filed in this or one or more separate applications.

Obviousness-type Double-Patenting Rejection

At page 2 of the Office Action, claim 28 was provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 28 of co-pending patent application Ser. No. 11/398,022. As the rejection is provisional, Applicant will address the rejection if patent application Ser. No. 11/398,022 is granted prior to the instant application and the claims of the instant application are otherwise in condition for allowance.

Rejection Under 35 USC §112, First paragraph (Enablement)

Claims 28, 30, 32, 33, 35, 36, 37, 41, 43, 48, 50, 52, 53, and 55-59 are rejected under 35 USC §112, first paragraph, as lacking enablement. In particular, the Office alleged that the claimed methods recite "haematological malignancy comprising a membrane androgen receptor" and that "[e]ven if one makes the assumption that B- and

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

T-cells bear such receptors, the fact is that all attempts to treat haematological malignancies by administering androgen receptor agonists have resulted in failure". The Office further took the position that "undue experimentation" would be required to practice the claimed invention. Applicant respectfully disagrees and traverses the rejection.

As an initial matter, Applicant notes that the Office has furnished no objective evidence to support its contention that it is a fact that all attempts to treat hematological malignancies with androgen receptor agonists have failed. Applicant has reviewed the art of record and can find no such statement. To the extent the instant rejection relies on this unsupported assertion, the Office has not met its burden of establishing a reasonable basis to question the enablement of the claimed invention.

On this ground alone, the instant rejection should be reconsidered and withdrawn.

However, even if the Office can provide some objective evidence showing that all attempts to treat hematological malignancies by administering androgen receptor agonists have failed, the evidence would not support the instant enablement rejection.

For instance, and as the specification makes quite clear, the claimed treatment methods feature solid or hematological cancers (malignancies) that include cells bearing the membrane androgen receptor (mAR). As the specification also makes abundantly clear, there are significant differences between the mAR and the receptor which binds the "androgen receptor agonists" referred to by the Office (referred to herein as the "classical androgen receptor"). See, for instance, Applicant's specification at page 1, line 18, to page 2, line 22 (disclosing, for instance, functional differences between the mAR and classical androgen receptor). In particular, the mAR and classical androgen receptor employ different biological pathways for activation. See the specification at page 1, lines 23-28, for instance.

Also, Applicant invites the Examiner's attention to art of record in this case, including Hatzogou, A., *et al.* (2005) *J. of Clinical Endo.* 90(2) 893 (disclosing, among other things, differences between the mAR and androgen receptor). This paper discloses related mouse experiments in which a particular steroid androgen conjugate

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

(testosterone-BSA) reduced LNCaP tumor size by 60% in nude mice. These results indicate that the claimed method can be used to treat cancer.

Clearly, the mAR and androgen receptor are different receptors. Whether or not others have treated hematological cancers with androgen receptor agonists is immaterial to the question of patentability in this case. On this ground alone, the rejection should be reconsidered and withdrawn.

For reasons already of record and the following, Applicant's specification fully satisfies the "how to make" and "how to use" requirements of 35 USC §112, first paragraph.

For example, and as is evident from the specification, Applicant identified the mAR in a variety of cells associated with hematological malignancies (cancers). See specification at page 27, line 21 to page 31, line 5. In particular, Applicant found expression of the mAR in several classes of white blood cell (WBC, see Table 1, page 28), various lymphocyte subclasses (Table 2, page 28) and in four cases of hematological malignancies (Tables 3-4, pages 29-30). Methods for making and using compositions for treatment that include androgen steroid covalently attached to a mammalian protein have been disclosed. See, for instance, page 7, lines 6-16 (disclosing particular methods of making the compositions, for instance), page 7, lines 17-19 (disclosing, for example, that the compositions may be used to treat hematological malignancies), page 8, lines 21 to page 9, line 11 (disclosing, among other things, preferred composition dosing regimens).

Citing the CCPA in *In re Marzocchi*, M.P.E.P. Section 2164.04 states, in pertinent part:

"...it is incumbent upon the Patent Office, whenever [an enablement] rejection...is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement...'439 F.2d at 224, 169 USPQ at 370". [Emphasis in original.]

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

Here, the Office does not offer "acceptable evidence or reasoning" to back up its assertions. Rather the Office proffers conclusory statements based on conjecture as grounds for alleging that the claims are not enabled. In contrast, Applicant has demonstrated in his patent specification as filed that the claims are enabled (see above, for instance). The art of record in this case supports this position (see, e.g., Hatzogou, A., et al.).

Accordingly, the invention of claims 28, 30, 32, 33, 35, 36, 37, 41, 43, 48, 50, 52, 53, 55-59 fully satisfies the enablement requirement of 35 USC §112, first paragraph. No "undue experimentation" is required to practice the invention. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Rejection under 35 USC §112, First Paragraph (Written Description)

Claims 28, 30, 32, 33, 35, 36, 37, 41, 43, 48, 50, 52, 53, 55-59 were rejected under 35 USC §112, first paragraph, as lacking written description. In particular, the Office took the position that "the issue here is whether there is any suggestion in the specification that leukemia or lymphoma is the direct result of androgen receptor bearing cells becoming malignant". The Office further alleged that "the suggestion that hematological malignancies comprise membrane androgen receptors lacks descriptive support in the specification". Applicant respectfully disagrees and traverses each ground of rejection.

Turning to the first ground, Applicant respectfully points out that the written description requirement of 35 USC §112, first paragraph, does not require a patentee to describe how or why a disease occurs before he can obtain a patent with claims to a method of treating it. Accordingly, the Office position that Applicant's specification must "suggest" that leukemia or lymphoma is the "direct result" of androgen receptor bearing cells becoming malignant is without merit or support in the statute. To the extent the instant rejection relies on this requirement, the Office has not satisfied its burden of providing a reasonable basis to challenge the adequacy of Applicant's written description.

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

As to the second ground, Applicant's specification provides ample written support that hematological malignancies include membrane androgen receptors (mAR). Some of that support has already been mentioned. For instance, Applicant identified the mAR in a variety of cells involved in hematological malignancies (cancers). See specification at page 27, line 21 to page 31, line 5. In particular, Applicant found expression of the mAR in several classes of white blood cell (WBC, see Table 1, page 28), various lymphocyte subclasses (Table 2, page 28) and in four cases of hematological malignancies (Tables 3-4, pages 29-30). Accordingly, there is ample descriptive support in the application as filed showing that hematological malignancies feature the mAR. Reconsideration and withdrawal of the rejection are thus requested.

Claims 30 and 44 are rejected as having typographical errors. Without acquiescing to the rejection and in order to expedite prosecution of the application, Applicant has amended claims 30 and 44.

Accordingly, claims 28 and 48, and all claims dependent therefrom, fully comply with the written description requirement of 35 USC §112, first paragraph. Therefore, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Rejection under 35 USC §112, Second Paragraph

Claims 28 and 48 are rejected under 35 USC §112, second paragraph, as being indefinite. Although Applicant respectfully disagrees with the stated basis for rejecting the claims, Applicant believes that the present submission addresses the rejection. In particular, the word "malignancy" has been deleted in favor of "cancer". Moreover, claims 28 and 48 have been amended to point out that the cancer includes cells that bear the membrane androgen receptor (mAR).

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection.

Claim Objections

Applicant notes that on the Office Action Summary page, Item 7, regarding disposition of the claims, indicates that claims 29, 44-47 and 49 are objected to.

U.S. Application Ser. No. 10/522,215
Amendment and Response

Docket No. 65321(54558)

Although the reasons for the objection to claim 44, and, presumably, claims 45-47, depending from claim 44, are given on page 5 of the Office Action, the reasons for the objection to claims 29 and 49 are not given. Applicant further notes that claims 29 and 49 are not subject to any of the pending rejections.

Therefore, Applicant can only conclude that claims 29 and 49 are objected to as being dependent upon a rejected based claim but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claim. Based on that conclusion, Applicant has added claims 60 and 61, wherein claim 60 is a combination of claim 28 and 29 and claim 61 is a combination of claims 48 and 49.

Request for Interview

Applicant respectfully requests a telephone interview with the Examiner before the Examiner issues the next Office Action. The undersigned will contact the Examiner to schedule the interview. Applicant thanks the Examiner in advance for the courtesy of an interview.

CONCLUSION

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of all rejections and allowance of the application with all pending claims. If a telephone conversation with Applicant's attorney would serve to expedite further prosecution of the application, Applicant invites the Examiner to contact the undersigned at the telephone number shown below.

Dated: November 14, 2007

Respectfully submitted,

By

Peter C. Lauro, Esq.

Registration No.: 32,360

EDWARDS ANGELL PALMER & DODGE LLP

P.O. Box 55874

Boston, Massachusetts 02205

(617) 439-4444

Attorneys/Agents For Applicant